

AM100788P1

SEQUENCE LISTING

<110> WYETH HOLDING CORPORATION.; KUNZ, ARTHUR ET AL.

<120> CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES

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Asn Tyr Trp Ile His

1 5

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Gly Ile Asn Pro Gly Asn Asn Tyr Thr Thr Tyr Lys Arg Asn Leu Lys

1 5 10 15

Gly

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Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr

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Arg Ser Ser Gln Ser Leu Ala Asn Ser Tyr Gly Asn Thr Phe Leu Ser

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Gly Ile Ser Asn Arg Phe Ser

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Leu Gln Gly Thr His Gln Pro Tyr Thr

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Asp Val Val Val Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Phe Gly

1 5 10 15

Asp Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Ala Asn Ser

20 25 30

Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Gln Ser

35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro

50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile

65 70 75 80

Ser Thr Ile Lys Pro Glu Asp Leu Gly Met Tyr Tyr Cys Leu Gln Gly

85 90 95

Thr His Gln Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

100 105 110

Arg

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<400> 8

Glu Val Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala

1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr

20 25 30

Trp Ile His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile

35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Thr Thr Tyr Lys Arg Asn Leu

50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Val Thr Ser Ala Ser Thr Ala Tyr

65 70 75 80

Met Asp Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys

85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly

100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser

115 120

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Gly Asn Asn Tyr Thr Thr Tyr Lys Arg Asn Leu Lys Gly

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Gly Asn Gln Tyr Thr Thr Tyr Lys Arg Asn Leu Lys Gly

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Gly Asn Asn Tyr Ala Thr Tyr Lys Arg Asn Leu Lys Gly

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Gly Asn Asn Tyr Val Thr Tyr Lys Arg Asn Leu Lys Gly

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Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Lys Arg Asn Leu Lys

1 5 10 15

Gly

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<223> K60R

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<400> 14

Gly Asn Asn Tyr Thr Thr Tyr Arg Arg Asn Leu Lys Gly

1 5 10

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<211> 17

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<223> CDR-H2 (K60R)R H"

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Gly Ile Asn Pro Gly Asn Asn Tyr Thr Thr Tyr Arg Arg Asn Leu Lys

1 5 10 15

Gly

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<213> Artificial Sequence

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Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu Lys

1 5 10 15

Gly

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<211> 70

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<213> Homo sapien

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<400> 17

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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Trp Tyr Gln Gln Lys Pro Gly Lys Ala

20 25 30

Pro Lys Leu Leu Ile Tyr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly

35 40 45

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp

50 55 60

Phe Ala Thr Tyr Tyr Cys

65 70

AM100788P1

<210> 18

<211> 11

<212> PRT

<213> Homo sapiens

<220>

<223> JK1

<220>

<221>

<400> 18

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg

1 5 10

<210> 19

<211> 113

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<213> Artificial Sequence

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<223> gL1

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<221>

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Asp Val Gln Val Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser Leu Ala Asn Ser

20 25 30

Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Lys Ala

35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro

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50 55 60  
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile  
65 70 75 80  
Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Gly  
85 90 95  
Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
100 105 110

Arg

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Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser Leu Ala Asn Ser  
20 25 30

Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Lys Ala  
35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro  
50 55 60

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Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile  
65                      70                      75                      80

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Gly  
                    85                      90                      95

Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
                    100                      105                      110

Arg

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<213> Homo sapiens

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<400> 21

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala  
1                      5                      10                      15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Trp Val  
                    20                      25                      30

Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Lys Phe Gln Gly  
                    35                      40                      45

Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met Glu  
                    50                      55                      60

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Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
65                70                75                80

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<213> Homo sapiens

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Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

1                5                10

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Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1                5                10                15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr

20                25                30

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Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile

35 40 45

Gly Gly Ile Asn Pro Gly Asn Gln Tyr Thr Thr Tyr Lys Arg Asn Leu

50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr

65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly

100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser

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<213> Artificial Sequence

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<223> gH4

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<221>

<400> 24

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr

20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile

AM100788P1

35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu

50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr

65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly

100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser

115 120

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<223> gH5

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Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr

20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile

35 40 45

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Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu  
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly  
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser  
115 120

<210> 26

<211> 121

<212> PRT

<213> Artificial Sequence

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<223> gH6

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<400> 26

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala  
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr  
20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile  
35 40 45



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Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe  
50 55 60

Gln Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly  
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser  
115 120

<210> 27

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<212> PRT

<213> Artificial Sequence

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<223> gH7

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<400> 27

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala  
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr  
20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile  
35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe

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50 55 60

Gln Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr

65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly

100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser

115 120

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<211> 239

<212> PRT

<213> Artificial Sequence

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<223> Full sequence of grafted light chain

<220>

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<400> 28

Met Lys Leu Pro Val Arg Leu Leu Val Leu Leu Leu Phe Trp Ile Pro

1 5 10 15

Ala Ser Arg Gly Asp Val Gln Val Thr Gln Ser Pro Ser Ser Leu Ser

20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser

35 40 45

Leu Ala Asn Ser Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys

50 55 60

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Pro Gly Lys Ala Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe  
65                      70                      75                      80

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe  
                    85                      90                      95

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr  
                    100                      105                      110

Cys Leu Gln Gly Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys  
                    115                      120                      125

Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro  
                    130                      135                      140

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu  
145                      150                      155                      160

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp  
                    165                      170                      175

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp  
                    180                      185                      190

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys  
                    195                      200                      205

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln  
                    210                      215                      220

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys  
225                      230                      235

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<212> DNA

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<223> Full sequence of grafted light chain

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<223> Full sequence of grafted heavy chain

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Met Asp Phe Gly Phe Ser Leu Val Phe Leu Ala Leu Ile Leu Lys Gly

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1 5 10 15

Val Gln Cys Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys

20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe

35 40 45

Thr Asn Tyr Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu

50 55 60

Glu Trp Ile Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg

65 70 75 80

Arg Lys Phe Gln Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser

85 90 95

Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val

100 105 110

Tyr Tyr Cys Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala

115 120 125

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys

130 135 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu

145 150 155 160

Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro

165 170 175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr

180 185 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val

195 200 205

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Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn  
210 215 220

Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser  
225 230 235 240

Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly  
245 250 255

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met  
260 265 270

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln  
275 280 285

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val  
290 295 300

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr  
305 310 315 320

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly  
325 330 335

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile  
340 345 350

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val  
355 360 365

Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser  
370 375 380

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu  
385 390 395 400

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Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro  
405 410 415

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val  
420 425 430

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met  
435 440 445

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser  
450 455 460

Leu Gly Lys  
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<223> 544gH1 T3

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<400> 34

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21

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tacctgcaca agcctggcca gtctccacag ctctcatct atgggatttc caacagattt 180  
tctgggggtgc cagacagggt cactggcagt gggtcaggga cagatttcac actcaagatc 240  
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atggacctca gcagcctgac aagtgaggac tctcggtct attactgtac aagagagggc 300  
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